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EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,137	SITAR, GIAMMARIA	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-12,14-21 and 25-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8-12,14-21 and 25-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-6, 8-12, 14-21 and 25-28 as amended (1/03/2006) are pending and under examination. Claims 2, 7, 13 and 22-24 were canceled by applicant.

Claim Rejections - 35 USC § 112

Indefinite

Claims 20, 21, and 28 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20, 21, and 28 remain/are indefinite with respect to the claimed phrase "a single separation step". The claimed method encompasses at least two steps including step of forming a non-physiological mixture of a blood sample and step of centrifugation. Thus, the claimed method does not appear to be one (single) step separation method. In alternative, the method comprises identification of NRBCs in the whole low density fraction of nucleated cells comprising NRBCs together with at least some lymphocytes and monocytes. Thus, the scope of claims does not appear to encompass a "single separation step" of nucleated cells because the claimed method includes at least two steps such as step of removal of one mixed cellular fraction and step of identification of various cells in one removed mixed cellular fraction.

Scope of enablement

Claims 11, 12, 14-21 and 25-28 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ascertaining the presence of fetal NRBCs in the whole low density fraction of nucleated cells comprising NRBCs, lymphocytes and

monocytes, does not reasonably provide enablement for a separation of NRBCs from lymphocytes and monocytes in blood. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Nature of the invention relates to detection of fetal cells circulating in maternal blood as intended for prenatal diagnosis (specification page 1).

Breadth of the claims is drawn to a separation of NRBCs from lymphocytes and monocytes in a mixture comprising maternal blood sample.

Amount of guidance and working examples are limited. There is one example describing removal of a low-density cellular fraction (density <1.068 g/ml) floating at the interface between plasma and medium after centrifugation that is enriched in fetal cells (page 10, lines 17-20). The low-density cellular fraction is said to contains "most" NRBCs present in starting blood **together** with "some" lymphocytes and monocytes as disclosed (page 10, lines 13-20). Thus, the specification clearly fails to describe a physical separation of NRBCs from lymphocytes and monocytes. No quantitative analysis for physical separation of NRBCs from lymphocytes and monocytes is disclosed. The specification fails to describe amounts of NRBCs, lymphocytes and monocytes in the separated fractions including amounts identified by terms "most" and "some. The final product contains more or less NRBCs together with more or less lymphocytes and monocytes as disclosed.

The prior art (IDS reference; Sitar et al. Hematologica. 1997, 82; 5-10) and the applicant's admission demonstrate that the densities of NRBCs, lymphocytes and monocytes are overlapping (instant specification page 3). The ranges of cell densities for NRBCs, lymphocytes

and monocytes include density <1.068 g/ml that are used in the instant method (page 10). Thus, the state of the prior art demonstrates unpredictability in physical separation of NRBCs from lymphocytes and monocytes due to their overlapping density ranges.

Furthermore, the specification describes that the starting mixture for cell separation is made by combining maternal blood with a culture medium and ACD (acid-citrate-dextrose, page 9) in order to form a "non-physiological" conditions as disclosed on page 9 or 5. The "non-physiological" conditions are believed to decrease the density of NRBCs and to increase the density of lymphocytes and monocytes (page 5, lines 10-15). However, this is not shown by applicant and no quantitative analysis for physical separation of NRBCs from lymphocytes and monocytes is disclosed by applicant. The claimed invention encompasses limitations drawn the use of generic "non-physiological" mixture(s) or conditions including the use of one singled out condition such as a low pH condition as claimed. However, no single condition from those that are described is clearly pointed as being critical for modifying the cell density (page 5). No quantitative analysis is disclosed for physical separation of NRBCs from lymphocytes and monocytes that would result from using "non-physiological" conditions including low pH as claimed. Moreover, no comparative showing with "physiological" conditions is disclosed.

Thus, the concept of a separation of NRBCs from lymphocytes and monocytes by using either generic "non-physiological" conditions or one singled-out low pH condition is not being enabled. Applicant demonstrates only the presence of fetal cells in the mixed low-density maternal blood cell fraction (table 3) but not a physical separation of NRBCs from lymphocytes and monocytes in maternal blood.

The prior art and applicant's admission demonstrates that densities of NRBCs, lymphocytes and monocytes are overlapping (page 3). Thus, the state of the prior art demonstrates unpredictability in separation of NRBCs from lymphocytes and monocytes. The criticality of generic "non-physiological" conditions for cell separation as claimed is not supported by quantitative showing as disclosed. The criticality of a low pH as a single "non-physiological" condition is not shown applicant.

Therefore, neither specification nor the prior art can be said to support the enablement of the claims over their breath.

Undue experimentation would be required to practice the invention as claimed due to the amount of experimentation necessary because of the limited amount of guidance and limited number of working examples in the specification, the nature of the invention, the state of the prior art, breadth of the claims and the unpredictability of the art.

As set forth in *In re Fisher*, 427 F2.d 833, 839, 166 USPQ 18, 24 (CCPA) 1970: [Section 112] requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of the enablement varies inversely with the degree of unpredictability of the factors involved. *Ex parte Humphreys*, 24 USPQ2d, 1260.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 1, 3-5, 8, 10-12, 14-21 and 25-28 as amended remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,641,628 (Bianchi) taken with US 5,676,849 (Sammons et al.); US 5,432,054 (Saunders et al.) and Guyton (Textbook of Medical Physiology. 8th edition. 1991, pages 276-280, 330-31, 752) as explained in the prior office action and repeated herein.

Claims are directed to a method for ascertaining the presence of fetal nucleated red blood cells (NRBCs) in maternal peripheral blood for prenatal genetic investigation wherein the method comprises step of combining a maternal blood sample with a medium in order to form a "non-physiological" mixture having specific characteristics that are pH 6.4-6.6, osmolarity 300-330 mOsm, Na^+ 150-160 mmol/l, K^+ 4.5-5.5 mmol/l, Cl^- 100-115 mmol/l, Ca^{++} 1.00 –2.50 mmol/l, glucose 400-500 mg/dl, lactate 10-20 mg/dl; step of transferring the mixture to a cell separation device and adding a high density liquid containing a red blood cell aggregating agent, step of isolating NRBCs by subjecting the separation device to centrifugal force, step of washing and resuspending the isolated NRBCs and step of ascertaining the presence of fetal NRBCs. Some claims are further drawn to the use of a liquid containing a red blood cells aggregating agent such as Ficoll-containing preparation. Some claims are further drawn to the use of a liquid in separation device with 1.068 g/ml density. Some claims are further drawn to the use a cell separation device or apparatus in a method for isolating fetal cells present in maternal peripheral blood for prenatal genetic investigation.

The cited patent US 5,641,628 (Bianchi et al.) is relied in the instant office action for the disclosure of methods for isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation (example 10) wherein the method encompasses isolation of fetal nucleated red blood cells by density gradient centrifugation of maternal blood which has

been modified by addition of a medium or citrate dextrose solution (col. 22, line 42). The cited patent also teaches steps of transferring the mixture to a cell separation device, adding a high density liquid with Ficoll, step of isolating fraction with mononuclear cells including NRBCs by subjecting the separation device to centrifugal force, step of washing and resuspending the isolated cells and step of identifying fetal NRBCs or ascertaining the presence of fetal NRBCs with antibodies to precursors of hematopoietic cells, by PCR techniques with Y chromosome primers (example 10) and detecting fetal hemoglobin (col. 4, line 36). .

The cited patent US 5,641,628 (Bianchi) discloses step of mixing maternal blood sample with citrate dextrose solution but it is silent with regard to the final characteristics of the modified blood mixture. However, the presently claimed amounts of Cl^-, Ca^{++} and lactate in the "non-physiological" mixture are the same as in a normal blood as evidenced by Guyton (page 277). Thus, the blood sample in the method of the cited patent US 5,641,628 (Bianchi) provides for the same amounts for Cl^-, Ca^{++} and lactate in the resulting blood mixture as encompassed by the claimed invention. The reference by Guyton also demonstrates that osmolarity of normal blood is about 302 mOsm that is within the presently claimed range. Thus, the blood sample of the cited patent US 5,641,628 (Bianchi) provides for the same osmolarity as encompassed by the claimed invention. Or, osmolarity in the method of US 5,641,628 (Bianchi) is reasonably expected to be increased after addition of citrate-dextrose solution. Although the presently claimed amounts for Na^+ and K^+ are slightly higher than in normal blood according to the reference by Guyton, however, the citrate-dextrose aqueous solution of the cited patent US 5,641,628 (Bianchi) is likely to provide for some additional sodium and/or potassium because citrate is commonly used in form of sodium/potassium salts in the solutions used for treatment of

blood samples. In alternative, the cited patent US 5,641,628 (Bianchi) also suggests that the blood sample is stored overnight with RPMI culture medium (col. 13, line 42) and, thus, the blood sample is reasonably expected to contain about the same amounts of potassium and/or sodium derived from basic RPMI. The cited patent US 5,641,628 (Bianchi) is silent about pH value of the final mixture. But US 5,676,849 (Sammons et al.) demonstrates that the commonly used citrate-dextrose/glucose aqueous solution including that is used in the method of US 5,641,628 (Bianchi) contains citric acid (col. 6, line 58 or col. 10, lines 39) and, therefore, is acidic. Thus, the common acid-citrate-dextrose solution in the method of US 5,641,628 (Bianchi) is reasonably expected to provide lowering pH in the final mixture and the final mixture would have pH lower than neutral pH of original blood sample in the method for fetal cells preparation or identification. Therefore, the blood mixture subjected to centrifugation in the method of US 5,641,628 (Bianchi) has substantially same characteristics as the blood mixture in the claimed method.

The cited patent US 5,641,628 (Bianchi) teaches the separation of cells by density centrifugation using Ficoll but it is silent about solution density in the method for separation of fetal cells from maternal blood. However, the cited patent US 5,432,054 (Saunders et al) teaches the use of liquid density gradient centrifugation for separation of fetal cells from maternal blood wherein the liquid density gradient includes 1.065 g/ml (col. 12, table 2) or about 1.068 g/ml for centrifugation of modified maternal blood as encompassed by the presently claimed method.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to practice a method for isolating fetal cells present in maternal peripheral blood for prenatal genetic investigation wherein the method encompasses isolation of

fetal nucleated red blood cells by density gradient centrifugation of maternal blood modified by addition of acid-citrate-dextrose (glucose) preparation as taught and suggested by the cited patents US 5,641,628 (Bianchi) and US 5,676,849 (Sammons et al.) with a reasonable expectation of success in isolating fetal nucleated red blood cells as demonstrated by the cited patents. The concept of isolating fetal cells from maternal blood of the cited patents US 5,641,628 (Bianchi), US 5,676,849 (Sammons et al.) and US 5,432,054 (Saunders et al.) is based on a density gradient centrifugation isolation of fetal nucleated red blood cells in low density cell fraction from modified maternal blood and it is similar to the concept of the presently claimed method which is also based on a density gradient centrifugation isolation of fetal nucleated red blood cells from modified maternal blood. The characteristics of the resulting modified blood sample that are claimed appear to be about the same as encompassed by the cited US 5,641,628 (Bianchi et al.) as evidenced by Guyton. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary. One of skill in the art would have been motivated to used acid-citrate-dextrose solution (ACD) for the expected benefits in blood cell separation because addition of ACD is a common practice in the methods for separation of fetal cells from maternal blood as adequately demonstrated by the cited US 5,641,628 (Bianchi) and US 5,676,849 (Sammons et al.). Thus, the claimed subject matter fails to patentably distinguish over the state art as represented be the cited references.

Therefore, the claims are properly rejected under 35 USC § 103.

2. Claims 1, 3-5, 8, 10-12, 14-21 as amended and new claims 25-28 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,641,628 taken with US 5,676,849; US

5,432,054 and Guyton as applied to claims 1, 3-5, 7 and 8 above, and further in view of US 4,424,132; GB 2-75376 and FR 77 08053 as explained in the prior office action and repeated herein.

Claims 1, 3-5, 8, 10-12, 14-21 and 25-28 as explained above. Claims 6 and 9 are further drawn to the use of a cell separation device or apparatus with elongated chamber and channel(s) that are open to the chamber in a method for isolating fetal cells present in maternal peripheral blood for prenatal genetic investigation.

The cited patents US 5,641,628; US 5,676,849 and US 5,432,054 are relied upon as explained above for the disclosure of methods for isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation wherein the methods encompass isolation of fetal nucleated red blood cells by density gradient centrifugation of modified maternal blood in various cell separation devices. The cited patents are silent about design of the cell separation devices. Nevertheless, the methods of the cited patents encompass the use of generic cell separation devices and they result in successful separation of fetal cells. Thus, there is a reasonably believe that the cell separation devices of the cited patents are suitable and appropriate in the methods for isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation.

Additional references US 4,424,132; GB 2-75376 and FR 77 08053 are relied upon to demonstrate a large variety of cell separation devices available in the prior art and suitable for cell separation in the present invention directed to a method for isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation. The devices of the cited patents comprise an elongated chamber and channel(s) that are open to the chamber.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use a large variety of cell separation devices suitable for separating blood cells including isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation as demonstrated by the cited references. The cited references are in the same field of endeavor and seek to solve the same problems as the instant application and claims such as blood cell separation, and one of skill in the art is free to select devices available in the prior art. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary. Moreover, the devices disclosed by the cited patents US 4,424,132; GB 2-75376 and FR 77 08053 are admitted by applicant as suitable in the presently claimed invention (specification page 6, par. 3). Thus, whatever differences might exist between various cell separation devices of the prior art and the particular device of the present invention, the claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 1/03/2006 have been fully considered but they are not all found persuasive.

With regard to the claim rejection under 35 U.S.C. 112, second paragraph, applicants argues (response page 9) that the claimed "single separation step" is certain because claimed invention encompasses the use of a single separation device. Yet, at the very least the rejected claims 21 and 28 are not so limited. The methods of claims 21 and 28 do not comprise the use of

any device(s). Although the method of claim 20 comprises the use of a separation device (see step b in preceding claim 1), however, the use of a "single" device does not necessarily mean application of one separation step. The scope of "a single separation step" as claimed is uncertain particularly in view that the claimed "low density cell fraction" comprises a mixture of cells.

With regard to the claim rejection under 35 U.S.C. 112, first paragraph, applicants argues (response pages 10-12) that the claimed invention uses a generic term such as "non-physiological" conditions as an umbrella term for a wide host of conditions and that one of skill in the art could vary these conditions by routine experimentation to practice the entire scope of invention as claimed. This is not found convincing because the scope of claims encompasses a separation of fetal cells from maternal lymphocytes and monocytes but the amount of guidance in the specification demonstrates possession of a mixed cell fraction comprising fetal cells together with maternal lymphocytes and monocytes. The state of art demonstrates that fetal nucleated red blood cells, lymphocytes and monocytes have overlapping cell densities. Thus, in the lack of knowledge about some specific separation conditions undue experimentation would be required to practice the invention as claimed due to the amount of experimentation necessary to screen for a wide host of conditions as argued. Moreover, the instant application fails to demonstrate how the density of cells are modified upon manipulation of any and all "non-physiological" conditions including one singled-out pH condition.

As related to claim rejection under 35 U.S.C. 103(a) applicants argue (response page 12) that the cited prior art does not teach and suggest all the claim limitation, in particular limitations of claims 6, 9, 26 and 27.

With respect to claims 6 and 9, it is noted that these claims are directed to the use of a device with some specific design. However, applicant does not provide any argument how the claimed device might be different from the cited prior art devices in the method for ascertaining the presence of fetal cells. Thus, Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references. Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections.

With respect to claims 26 and 27, it is noted that these claims are directed to the amount of analyzed nucleated cells such as "13767 or less". However, the cited prior art appears to disclose analyzing the same amounts of separated fetal cells. For example: see US 5,432,054 (table 1) or see US 5,676,849 (table 1) wherein the disclosed numbers of separated and analyzed fetal nucleated cells are within the claimed ranges. Thus, Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references. Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks

the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections.

Some of the applicant's arguments are directed to the concept of a separation of NRBCs from lymphocytes and monocytes (response page 12-14). Yet, the present application fails to demonstrate the separation of cells as argued and as claimed. The main argument is directed to the idea that the presently claimed invention, in particular claims 11 and 25, is/are patentably distinct from the cited prior art on the basis on the pH range in the mixture of blood sample and that the prior art does not recognize pH value as the result effective variable.

This argument is not found particularly convincing because the use of ACD (acid citrate dextrose solution) in the method of US'628 (Bianchi et al.) lead to the same "non-physiological" conditions within the meaning of the claims as explained above. Further, the argument is not found particularly convincing in the lack of evidence that pH is a critical condition in the "non-physiological" mixture that would result in separation of cells. The as-filed specification does not provide evidence related to pH criticality and it does not demonstrate that lowering pH causes separation of fetal NRBCs from maternal lymphocytes and monocytes. Although some different amounts of ACD (acid-citrate-dextrose) could be used in the prior art method for modifying blood samples, the use of at least some amounts of ACD (acid-citrate-dextrose solution) is reasonably expected to provide for somehow lower pH than physiologically normal pH. Moreover, the cited prior art methods have been successful in detecting presence of fetal NRBCs in the low-density cell fractions that are removed by centrifugation of blood samples in separating media including Ficoll.

Applicant also argues that the cited patent by Bianchi et al. teaches away from the claimed invention because it describes the method resulting in a "mononuclear cell layer" and thus, there is no teaching about separation of fetal cells from lymphocytes and monocytes. However, the claimed method results in a mixed cell fraction that "comprises" fetal cells as claimed (claim 1). The applicant's method results in a mixed cell fraction comprising fetal cells together with lymphocytes and monocytes as disclosed (page 10, line 19).

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

March 13, 2006

VERA AFREMOVA

PRIMARY EXAMINER